

Inspiratory Muscle Training for Patients With Chronic Obstructive Pulmonary Disease: A Practical Guide for Clinicians

Kylie Hill, PhD, Nola M. Cecins, MSc, Peter R. Eastwood, PhD, Sue C. Jenkins, PhD

ABSTRACT. Hill K, Cecins NM, Eastwood PR, Jenkins SC. Inspiratory muscle training for patients with chronic obstructive pulmonary disease: a practical guide for clinicians. *Arch Phys Med Rehabil* 2010;91:1466-70.

Reduced inspiratory muscle strength is common in people with chronic obstructive pulmonary disease (COPD) and is associated with dyspnea and decreased exercise capacity. Most studies of inspiratory muscle training (IMT) in COPD have demonstrated increased inspiratory muscle strength. Many have also shown improvements in dyspnea and exercise capacity. However, a persisting challenge when translating and applying the findings of these studies in clinical practice is the disparity in training loads, modalities, and outcomes measures used in the different studies. This commentary summarizes our clinical and research experience with a threshold IMT device with the aim of providing clinicians interested in prescribing IMT in this population with practical recommendations regarding patient selection, assessment, and implementation of training. We propose using an interval-based high-intensity threshold IMT program for people who are unable to participate fully in whole-body exercise training because of comorbidities such as severe musculoskeletal problems. Initial training loads equivalent to at least 30% of a person's maximum inspiratory pressure (P_{lmax}) are required for all people undertaking IMT. Supervision, which includes monitoring of oxygen saturation throughout the first training session, is recommended, and patients are warned to expect transient delayed-onset muscle soreness, a consequence of muscle adaptation to an unaccustomed activity. We recommend training be undertaken 3 times a week for 8 weeks, with loads progressively increased as symptoms permit. It is prudent to exclude people at risk of pneumothorax or spontaneous rib fracture. Evaluation of IMT should include measures of P_{lmax}, dyspnea, health-related quality of life, and exercise capacity.

Key Words: Pulmonary disease, chronic obstructive; Rehabilitation.

© 2010 by the American Congress of Rehabilitation Medicine

From the School of Physiotherapy and Curtin Health Innovation Research Institute, Curtin University, Perth, Australia (Hill, Cecins, Eastwood, Jenkins); Physiotherapy Department (Cecins, Jenkins), Department of Pulmonary Physiology (Eastwood), Sir Charles Gairdner Hospital, Perth, Australia; Lung Institute of Western Australia and Centre for Asthma, Allergy and Respiratory Research (Hill, Cecins, Jenkins), School of Anatomy and Human Biology (Eastwood), University of Western Australia, Perth, Australia.

Supported by a National Health and Medical Research Council Senior Research Fellowship (grant no. 513704).

No commercial party having a direct financial interest in the results of the research supporting this article has or will confer a benefit on the authors or on any organization with which the authors are associated.

Reprint requests to Kylie Hill, PhD, School of Physiotherapy, Curtin University, GPO Box U1987, Perth, 6845 Western Australia, e-mail: K.Hill@curtin.edu.au.

0003-9993/10/9109-00544\$36.00/0

doi:10.1016/j.apmr.2010.06.010

IN PEOPLE WITH CHRONIC obstructive pulmonary disease, inspiratory muscle dysfunction arises largely as a consequence of the mechanical effects of pulmonary hyperinflation on the diaphragm.¹ The increased gas volume in the lungs at the end of expiration places the diaphragm at a mechanical disadvantage, thereby impairing its length-tension relationship and reducing its maximum pressure-generating capacity (ie, strength).² Reduced inspiratory muscle strength in people with COPD has been associated with dyspnea and decreased exercise capacity.^{3,4} A corollary of this is that improvements in inspiratory muscle strength could decrease dyspnea and increase exercise capacity in these patients.

To date, over 20 studies have investigated the effect of IMT in COPD. The results of these studies have been reported in systematic reviews⁵⁻⁷ that used well defined search strategies and undertook meta-analyses with the methods described by the Cochrane Collaboration.⁸ However, the translation and application of these research findings into clinical practice are challenging because patients who are commonly referred to pulmonary rehabilitation programs, such as those with comorbid conditions,⁹ are usually excluded from studies of IMT.¹⁰⁻¹³ Furthermore, many studies have used assessment procedures that require access to equipment and familiarity with test protocols that are beyond the scope of routine clinical practice.¹⁰⁻¹⁴ Also, information regarding specific criteria used to guide progression of training loads or maintenance strategies, both essential for clinical application of IMT, is rarely provided in these research-orientated studies.

The aim of this commentary is to provide health care professionals interested in prescribing IMT for people with COPD with practical recommendations to facilitate the translation of research findings into clinical practice. To achieve this aim, we integrate the results of previous research pertaining to IMT in COPD together with our clinical experience using a threshold IMT device in this population.^{15,16} Our recommendations are provided with regard to patient selection, contraindications, assessment, safety, and supervision requirements. We provide specific details of an IMT program, including the prescription of initial training loads, guidelines for progression, and maintenance strategies. These recommendations are summarized in table 1.

List of Abbreviations

COPD	chronic obstructive pulmonary disease
FRC	functional residual capacity
HRQOL	health-related quality of life
IMT	inspiratory muscle training
P _{lmax}	maximum inspiratory pressure
RPE	Rating of Perceived Exertion
RV	residual volume
SpO ₂	oxygen saturation as measured by pulse oximetry

Table 1: Clinical Recommendations for IMT in Patients With COPD

Recommendation	Clinical Rationale
Patient selection and safety	
Consider for people who are unable to participate fully in WBET because of comorbid conditions such as severe musculoskeletal problems or claudication.	Given the strong evidence of WBET in COPD, ¹⁷ IMT should be considered an adjunct to, not a replacement for, WBET. The current evidence does not support the routine addition of IMT to a program of WBET. ¹⁹ It likely to be most appropriate for those who are unable to achieve the full benefits of WBET.
Consider for people who achieve minimal improvement in dyspnea or exercise capacity after a program of WBET.	There is strong evidence that IMT, when applied in isolation, reduces dyspnea. ^{5,7} Therefore, IMT might be appropriate for those who have ongoing intractable dyspnea despite completing WBET.
Exclude people at risk of spontaneous pneumothorax or rib fractures.	IMT necessitates the generation of large negative intrathoracic pressures; therefore, people who are at risk of spontaneous pneumothorax or rib fractures should be excluded from participation.
Supervise the first training session and monitor respiratory rate and oxygen saturation.	The only strategy to minimize the load imposed with a threshold loading device is to hypoventilate. ¹⁶ Therefore, the first training should be supervised and respiratory rate and oxygen saturation monitored to ensure that patients are not hypoventilating during loaded breathing.
Assessment	
Before and after a program of IMT, measure P _{lmax} , dyspnea, exercise capacity, and HRQOL.	The measurement of P _{lmax} allows the prescription of an appropriate initial training load. Dyspnea, exercise capacity, and HRQOL are likely to be important to the patient and therefore should be measured to evaluate the effectiveness of the program of IMT.
Training program	
Use a threshold IMT device.	These devices are simple and inexpensive, and the load that is imposed is largely independent of the breathing pattern adopted by the patient. ³⁷
Consider an interval-based training program 3 times/wk for 8wk.	Interval-based training allows the training load that can be tolerated to be optimized. ¹⁶ It also minimizes any decrease in oxygen saturation during loaded breathing.
Initial loads should be $\geq 30\%$ P _{lmax} .	Loads $< 30\%$ of P _{lmax} are insufficient to induce a training adaptation. ³⁴
Progress according to perceived exertion such that patients describe training as somewhat hard (between 12 and 14) on the RPE scale. ³²	As with WBET, loads must be progressively increased to optimize the benefit. Progression is most easily done according to the RPE during training.
Reassessment and maintenance	
If after 8wk of training, dyspnea, exercise capacity, and HRQOL are unchanged, considering ceasing IMT.	Motivation for people to continue with IMT will be based on changes in outcome measures that are perceived by them to be important, such as reductions in dyspnea or improvements in exercise capacity and HRQOL.
A maintenance training program should continue for at least 2 sessions each week.	Without adherence to a maintenance program, training-related gains are lost within 12mo. ⁴¹

Abbreviation: WBET, whole-body exercise training.

PATIENT SELECTION

Pulmonary rehabilitation that includes supervised whole-body exercise training has achieved strong evidence for reducing dyspnea, improving HRQOL, and increasing exercise capacity.¹⁷ Several studies have investigated whether the addition of IMT to a program of whole-body exercise training offers benefits above those seen after whole-body exercise training in isolation.¹⁸ The results, when combined in meta-analyses, have demonstrated additional gains in inspiratory muscle strength and endurance but not dyspnea, HRQOL, or exercise capacity.^{5,6} Therefore, in people who are able to participate fully in whole-body exercise training, current evidence does not support the routine use of IMT.¹⁹ Nevertheless, recent meta-analyses provide strong evidence that IMT, when applied in isolation to patients with moderate-to-severe COPD, results in large reductions in dyspnea^{5,7} (> 2 points on the Transitional Dyspnea Index).²⁰

When applied in isolation, IMT may also confer an increase in functional exercise capacity.⁷ Therefore, IMT should be

considered a treatment option for people who are unable to participate fully in whole-body exercise training because of comorbid conditions such as severe musculoskeletal problems or claudication. Patients who achieve minimal improvement in dyspnea or exercise capacity after a program of whole-body exercise training may also benefit from IMT. However, further study is needed to confirm this contention.

Contraindications, Safety, and Supervision

Most studies of IMT exclude patients with COPD who require long-term oxygen therapy, or with a history of recent exacerbation or significant comorbid cardiovascular or neurologic conditions.^{13,16,21} Because IMT necessitates the generation of substantial negative intrathoracic pressure, it is prudent to exclude people at risk of spontaneous pneumothorax or rib fractures. Specifically, we exclude people with (1) a recent undrained pneumothorax or history of recurrent spontaneous pneumothorax, (2) large bullae on chest radiograph, (3) marked

osteoporosis together with a history of spontaneous rib fractures, or (4) a history of recent lung surgery (ie, within 12mo).

To ensure the safety of patients when initiating IMT, we recommend that the first training session be supervised. Because breathing against an external inspiratory load is an unaccustomed activity, it may result in delayed onset muscle soreness, signifying the normal damage and repair processes necessary for muscle adaptation to a training stimulus.²² However, people should be advised to stop training immediately and seek medical attention if they experience severe sharp pain on inspiration. A modest decrease in arterial oxygen saturation measured using pulse oximetry (SpO₂, eg, to 94%) has been reported among people with COPD when breathing against inspiratory loads that were incremented each minute until symptom limitation.²³ This most likely reflects the onset of hypoventilation as a strategy to minimize the load imposed using a threshold device, particularly when the load approaches the maximum that the person can achieve.^{16,24} The use of an interval-based protocol (see "The Training Program") allows a rest or recovery period to occur, which can serve to minimize the decrease in SpO₂ during the loaded breathing protocol. Nevertheless, we recommend monitoring of respiratory rate and SpO₂ during the initial training sessions to evaluate the response to loaded breathing.

EVIDENCE FOR HIGH-INTENSITY INTERVAL-BASED IMT

As with other skeletal muscles, improvements in strength are likely to be dose-dependent.²⁵ Constant load training protocols limit the load that can be achieved by people with COPD because of the rapid development of intolerable symptoms that necessitate resting.²⁶ As with interval-based whole-body exercise training, the application of an interval-based approach to IMT can optimize the load able to be tolerated by allowing regular rest periods and subsequent relief of symptoms.^{15,16} This, in turn, maximizes the potential improvement in strength and endurance of the inspiratory muscles.¹⁶

Compared with a control group that underwent sham training, the high-intensity interval-based IMT program described in this commentary has been shown to increase P_Imax and inspiratory muscle endurance, reduce dyspnea and fatigue, and improve functional exercise capacity measured using the six-minute walk test.¹⁶ While this study did not show a between-group difference in HRQOL, when the results were pooled with data from other studies of IMT applied in isolation, a significant improvement was demonstrated.⁷

PATIENT ASSESSMENT

Assessment prior to IMT requires measurements of inspiratory muscle function in addition to outcome measures such as dyspnea, exercise capacity, and HRQOL. In clinical practice, the P_Imax is often measured in respiratory medicine laboratories.²⁷ Small hand-held devices are also commercially available for this purpose.²⁸

The measurement of P_Imax involves the generation of a maximum inspiratory effort, sustained for more than 1 second, against an occluded airway.²⁷ Practice attempts are required because P_Imax improves significantly with familiarization.²⁹ Therefore, where possible, multiple measures need to be made on more than 1 occasion.¹⁶ Inspiratory efforts can be initiated from RV or FRC. Although P_Imax measured from RV is considered to be more stable than FRC, people with COPD frequently report considerable effort when expiring to RV, and this limits their capacity to tolerate repeated P_Imax measurements from this volume. Furthermore, in contrast with healthy

people who adopt the strategy of exhaling toward RV in an attempt to increase the mechanical advantage of the inspiratory muscles,³⁰ patients with COPD cannot manage this because of expiratory airflow limitation and breathe closer to the usual FRC during loaded breathing.²³ For these reasons, measurements of P_Imax initiated from FRC may be more relevant and feasible in patients with COPD. Regardless of which volume is chosen, it is essential that it remain consistent at all assessments.²⁷

Several protocols have been described to measure inspiratory muscle endurance using threshold loads.³¹ Most commonly, these protocols are characterized by the imposition of either incremental or constant submaximal inspiratory loads, sustained until symptom limitation.²⁴ Performance is dependent on the breathing pattern adopted,²⁴ and therefore, the measurement of inspiratory muscle endurance is complex and beyond the scope of usual clinical practice.

Although not ideal, in the absence of equipment to measure P_Imax, IMT can be initiated without a measurement of inspiratory muscle strength. In this situation, we recommend that initial loads are chosen that are perceived by the patient as somewhat hard (ie, between 12 and 14 on the RPE).³² Initial inspiratory threshold loads requiring the generation of approximately -20 cmH₂O are likely to be appropriate for most people with COPD.

Comparison of P_Imax before and after IMT allows clinicians to determine whether the training load was adequate to induce a training-related improvement in inspiratory muscle strength. A lack of change in P_Imax is likely to indicate inadequate training loads. However, large improvements in P_Imax are unlikely to be perceived as important by patients unless they coexist with meaningful improvements in dyspnea, exercise capacity, or HRQOL. Methods to evaluate these latter outcomes have been described elsewhere.³³ Long-term adherence to IMT is likely to be contingent on improvements in outcomes that are meaningful to the patient.

THE TRAINING PROGRAM

Modality Selection

We recommend the use of a threshold loading device to train the inspiratory muscles.¹⁶ The device is composed of a mouth-piece attached to a small plastic cylinder that contains a spring-loaded poppet valve. The valve opens to permit inspiratory flow only once the person has generated adequate negative intrathoracic pressure to condense the spring.³⁴ Although normocapnic hyperpnea and resistive loading devices have been described as training modalities, both have limitations that reduce their clinical usefulness. Specifically, normocapnic hyperpnea is a training approach that requires people to ventilate at a high proportion of their maximum voluntary ventilation for a fixed period using complicated rebreathing circuitry to ensure stable levels of carbon dioxide.³⁵ The use of a resistive load device requires close attention to breathing pattern because people can reduce the training load imposed by decreasing inspiratory flow.³⁶ In contrast, threshold loading devices impose an inspiratory load that is largely independent of breathing pattern.³⁷ They are simple to use, commercially available, and relatively inexpensive (<\$30USD).

Interval-Based Training

The IMT program used at our facility is based on a protocol previously demonstrated to be feasible¹⁵ and effective.¹⁶ Training takes place with the patient seated, wearing a nose clip. Patients are permitted to lean forward and fix their upper limbs

Patient's name: _____ Date IMT commenced: _____ Today's date: _____
 Baseline P_Imax: _____ Training session number: _____ Comorbid conditions: _____
 Resting SpO₂: _____ Resting dyspnea (0–10): _____

Training Interval Cycle: 2min work: 1min rest	Load (-cmH ₂ O)	No. of Breaths	Perceived Exertion (6–20)	Comments
1min warm-up				
Cycle 1				
Cycle 2				
Cycle 3				
Cycle 4				
Cycle 5				
Cycle 6				
Cycle 7				

End-session SpO₂: _____ End-session dyspnea (0–10): _____

Fig 1. Training record.

on the arms of chair or table if desired. Training commences with a 1-minute warm-up at 50% of the target inspiratory training load (see “Training loads”). Thereafter, an interval-based training approach is used, characterized by a work to rest ratio of 2 minutes (work) to 1 minute (rest). This 3-minute cycle is repeated 7 times, resulting in a 21-minute training session (ie, 14 minutes of loaded breathing). Patients are permitted to select their own breathing pattern, and expiration is unloaded. Training is undertaken 3 times a week for 8 weeks, and patients are encouraged to record their training sessions in an exercise diary. If feasible, we recommend that at least 1 training session is supervised each week in order to permit the training load to be increased when possible. For people who are unable to attend supervised sessions, adherence can be assessed via weekly phone contact and the training load increased according to patient feedback.

Training Loads

For the initial 2-minute interval, a training load is selected equivalent to 30% of a patient's P_Imax. Loads less than 30% of P_Imax are insufficient to induce improvement in inspiratory muscle strength.³⁴ Consistent with the current recommendations for whole-body exercise training,³⁸ we use a symptom-limited approach to guide the progression of training loads. We select loads that patients describe as somewhat hard—that is, between 12 and 14 on the RPE scale.³² Training loads are increased during the designated rest intervals to achieve these RPE targets. Patients train at loads corresponding to a higher RPE if tolerated and there are no abnormal signs (eg, marked oxygen desaturation) or symptoms (eg, prolonged delayed-onset muscle soreness).

On completion of the first training session, patients are often training at loads equal to approximately 40% of P_Imax. In our experience, the inspiratory load can usually be increased rapidly during the first 4 weeks of training, largely as a consequence of neurosensory adaptation³⁹ reflecting desensitization to the inspiratory loads and improved recruitment of motor units.^{25,40} Thereafter, the rate of increase often slows, and further increments in muscle function are likely to reflect gains resulting from muscular hypertrophy.¹³ An example of the record we use to monitor progress with the IMT program is provided (fig 1).

REASSESSMENT

Reassessment of all outcome measures is performed 8 weeks after the initiation of training. At this time, IMT is ceased if little improvement has occurred in dyspnea, exercise capacity, or HRQOL despite an increase in P_Imax.

MAINTENANCE

Training-related gains are lost within 12 months if regular IMT is ceased.⁴¹ In order to optimize the maintenance of benefits, we encourage the completion of at least 2 IMT sessions each week at the load achieved during the final session of the 8-week program. The role of IMT during an acute exacerbation of COPD is unknown; therefore, we cease both training and maintenance programs during these clinical events. As with whole-body exercise training, the training load used during IMT will need to be reduced after an exacerbation. Typically, the first session after an exacerbation is fully supervised the training load decreased to that selected for the initial training session. The subsequent rate of increase in training loads is usually more rapid than during the pre-exacerbation training period.

CONCLUSIONS

This report describes a practical approach to the initiation and progression of an IMT program for people with stable COPD. We advocate the use of a threshold loading device and a high-intensity interval-based training program. Our recommendations are based on current evidence and our clinical practice in this area.

References

- O'Donnell DE, Revill SM, Webb KA. Dynamic hyperinflation and exercise intolerance in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2001;164:770-7.
- Similowski T, Yan S, Gauthier AP, Macklem PT, Bellemare F. Contractile properties of the human diaphragm during chronic hyperinflation. *N Engl J Med* 1991;325:917-23.
- Hamilton AL, Killian KJ, Summers E, Jones NL. Muscle strength, symptom intensity, and exercise capacity in patients with cardiorespiratory disorders. *Am J Respir Crit Care Med* 1995;152:2021-31.
- Gosselink R, Troosters T, Decramer M. Peripheral muscle weakness contributes to exercise limitation in COPD. *Am J Respir Crit Care Med* 1996;153:976-80.

5. Lotters F, van Tol B, Kwakkel G, Gosselink R. Effects of controlled inspiratory muscle training in patients with COPD: a meta-analysis. *Eur Respir J* 2002;20:570-6.
6. O'Brien K, Geddes EL, Reid WD, Brooks D, Crowe J. Inspiratory muscle training compared with other rehabilitation interventions in chronic obstructive pulmonary disease: a systematic review update. *J Cardiopulm Rehabil Prev* 2008;28:128-41.
7. Geddes EL, O'Brien K, Reid WD, Brooks D, Crowe J. Inspiratory muscle training in adults with chronic obstructive pulmonary disease: an update of a systematic review. *Respir Med* 2008;102:1715-29.
8. Higgins JPT, Green S, editors. *Cochrane handbook for systematic reviews of interventions 4.2.6 [updated September 2006]: The Cochrane Library*. Chichester: John Wiley and Sons, Ltd; 2006. Issue 4.
9. Crisafulli E, Costi S, Luppi F, et al. Role of comorbidities in a cohort of patients with COPD undergoing pulmonary rehabilitation. *Thorax* 2008;63:487-92.
10. Larson JL, Covey MK, Wirtz SE, et al. Cycle ergometer and inspiratory muscle training in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1999;160:500-7.
11. Preusser BA, Winningham ML, Clanton TL. High- vs low-intensity inspiratory muscle interval training in patients with COPD. *Chest* 1994;106:110-7.
12. Sanchez Riera H, Montemayor Rubio T, Ortega Ruiz F, et al. Inspiratory muscle training in patients with COPD: effect on dyspnea, exercise performance, and quality of life. *Chest* 2001;120:748-56.
13. Ramirez-Sarmiento A, Orozco-Levi M, Guell R, et al. Inspiratory muscle training in patients with chronic obstructive pulmonary disease: structural adaptation and physiologic outcomes. *Am J Respir Crit Care Med* 2002;166:1491-7.
14. Mador MJ, Deniz O, Aggarwal A, Shaffer M, Kufel TJ, Spengler CM. Effect of respiratory muscle endurance training in patients with COPD undergoing pulmonary rehabilitation. *Chest* 2005;128:1216-24.
15. Sturdy G, Hillman D, Green D, Jenkins SC, Cecins N, Eastwood P. Feasibility of high-intensity, interval-based respiratory muscle training in COPD. *Chest* 2003;123:142-50.
16. Hill K, Jenkins SC, Philippe DL, et al. High-intensity inspiratory muscle training in COPD. *Eur Respir J* 2006;27:1119-28.
17. Lacasse Y, Goldstein R, Lasserson TJ, Martin S. Pulmonary rehabilitation for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2006;(4):CD003793. Review.
18. Hill K, Eastwood PR. Respiratory muscle training: the con argument. *Chron Respir Dis* 2005;2:223-4.
19. Ries AL, Bauldoff GS, Carlin BW, et al. Pulmonary rehabilitation: joint ACCP/AACVPR evidence-based clinical practice guidelines. *Chest* 2007;131:4S-42S.
20. Mahler DA, Weinberg DH, Wells CK, Feinstein AR. The measurement of dyspnea: contents, interobserver agreement, and physiologic correlates of two new clinical indexes. *Chest* 1984;85:751-8.
21. Heijdra YF, Dekhuijzen PN, van Herwaarden CL, Folgering TM. Nocturnal saturation improves by target-flow inspiratory muscle training in patients with COPD. *Am J Respir Crit Care Med* 1996;153:260-5.
22. Orozco-Levi M, Lloreta J, Minguella J, Serrano S, Broquetas JM, Gea J. Injury of the human diaphragm associated with exertion and chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2001;164:1734-9.
23. Sturdy GA, Hillman DR, Green DJ, Jenkins SC, Cecins NM, Eastwood PR. The effect of learning on ventilatory responses to inspiratory threshold loading in COPD. *Respir Med* 2004;98:1-8.
24. Hill K, Jenkins SC, Philippe DL, Shepherd KL, Hillman DR, Eastwood PR. Comparison of incremental and constant load tests of inspiratory muscle endurance in COPD. *Eur Respir J* 2007;30:479-86.
25. Kraemer WJ, Fleck SJ, Evans WJ. Strength and power training: physiological mechanisms of adaptation. *Exerc Sport Sci Rev* 1996;24:363-97.
26. Puhan MA, Busching G, Schunemann HJ, VanOort E, Zaugg C, Frey M. Interval versus continuous high-intensity exercise in chronic obstructive pulmonary disease: a randomized trial. *Ann Intern Med* 2006;145:816-25.
27. American Thoracic Society/European Respiratory Society. ATS/ERS statement on respiratory muscle testing. *Am J Respir Crit Care Med* 2002;166:518-624.
28. Hamnegard CH, Wragg S, Kyroussis D, Aquilian R, Moxham J, Green M. Portable measurement of maximum mouth pressures. *Eur Respir J* 1994;7:398-401.
29. Larson JL, Covey MK, Vitalo CA, Alex CG, Patel M, Kim MJ. Maximal inspiratory pressure. Learning effect and test-retest reliability in patients with chronic obstructive pulmonary disease. *Chest* 1993;104:448-53.
30. Eastwood PR, Hillman DR, Finucane KE. Ventilatory responses to inspiratory threshold loading and role of muscle fatigue in task failure. *J Appl Physiol* 1994;76:185-95.
31. Troosters T, Gosselink R, Decramer M. Respiratory muscle assessment. *Eur Respir Monogr* 2005;31:57-71.
32. Borg GA. Psychophysical bases of perceived exertion. *Med Sci Sports Exerc* 1982;14:377-81.
33. Zuwallack RL. Outcome measures for pulmonary rehabilitation. *Eur Respir Monogr* 2000;13:177-200.
34. Larson JL, Kim MJ, Sharp JT, Larson DA. Inspiratory muscle training with a pressure threshold breathing device in patients with chronic obstructive pulmonary disease. *Am Rev Respir Dis* 1988;138:689-96.
35. Belman MJ, Mittman C. Ventilatory muscle training improves exercise capacity in chronic obstructive pulmonary disease patients. *Am Rev Respir Dis* 1980;121:273-80.
36. Belman MJ, Thomas SG, Lewis MI. Resistive breathing training in patients with chronic obstructive pulmonary disease. *Chest* 1986;90:662-9.
37. Eastwood PR, Hillman DR. A threshold loading device for testing of inspiratory muscle performance. *Eur Respir J* 1995;8:463-6.
38. Nici L, Donner C, Wouters E, et al. ATS/ERS Pulmonary Rehabilitation Writing Committee. American Thoracic Society/European Respiratory Society statement on pulmonary rehabilitation. *Am J Respir Crit Care Med* 2006;173:1390-413.
39. Eastwood PR, Hillman DR, Morton AR, Finucane KE. The effects of learning on the ventilatory responses to inspiratory threshold loading. *Am J Respir Crit Care Med* 1998;158:1190-6.
40. Huang CH, Martin AD, Davenport PW. Effect of inspiratory muscle strength training on inspiratory motor drive and RREP early peak components. *J Appl Physiol* 2003;94:462-8.
41. Weiner P, Magadle R, Beckerman M, Weiner M, Berar-Yanay N. Maintenance of inspiratory muscle training in COPD patients: one year follow-up. *Eur Respir J* 2004;23:61-5.